

### **REMARKS**

Claims 1-65 and 70-74 are pending and under examination. Claims 66-69 are withdrawn from consideration as being directed to a non-elected invention. Applicants reserve the right to pursue these claims in a later filed application claiming the benefit of the subject application. By the present communication, no claims have been added or canceled, and claims 1, 30, 34 and 71 have been amended. Support for the amendments can be found throughout the application as filed. In particular, support for the amendment to claim 1 can be found in, for example, cancelled claim 17 and at, for example, paragraphs [0039], [0042]-[0043] and [0051]. Support for the amendment to claim 30 can be found at, for example, paragraph [0040]. Support for the amendment to claims 34 and 71 can be found at, for example, paragraphs [0042]-[0043], [0075]-[0084], Figures 1 and 5 and throughout the Examples. Accordingly, the amendments do not raise an issue of new matter.

Applicants thank Examiner Zeman for extending a personal interview on August 22, 2006, to Applicants' representatives and to Dr. Christophe Schilling, during which amendments were discussed that the Examiner indicated would likely be viewed favorably. The above amendments and remarks are believed to be consistent with the discussions during the interview.

### **Objections to the Specification**

Applicants respectfully traverse the objection to the specification under 37 C.F.R. §1.75(d)(1) as allegedly failing to provide proper antecedent basis for the subject matter of claims 12-13 and 46-45. The amendments to claims 30 and 35-38 filed December 29, 2005, have also been objected to under 35 U.S.C. §132(a) as allegedly introducing new matter. Because these objections appear to be substantially similar to the rejection of claims 12-13, 30, 35-38 and 46-45 of the current Office Action, for allegedly lacking written description, Applicants respectfully direct the Examiner's attention to the arguments provided below.

**Priority**

Priority of the claimed invention to either of provisional application serial numbers 60/272,754, filed March 1, 2001, or 60/323,028, filed September 14, 2001, has not been accorded to the subject application. The Office alleges that neither application describes a computer readable media as is claimed in claims 1-33, or a method of determining a systemic property as is claimed in claims 34-65 and 70-74.

As previously pointed out, the burden is not on Applicants in the first instance to show support for priority to an earlier application. Rather, the initial burden is on the Office. Nevertheless, to further prosecution of this application, Applicants respectfully submit that the priority applications describe throughout their specification, claims and drawings a computer readable medium or medium and a method as currently claimed. For example, with respect to a computer readable medium containing the claimed data structure and the method of predicting a systemic property of a biochemical reaction network, the '754 application teaches:

We describe the process of building mathematical models of microbial regulation and metabolism. From the annotated genome sequences and the experimentally determined biochemical and physiological characteristics for a given organism, its network of metabolic reactions can be reconstructed. The reconstructed metabolic network is then analyzed using various mathematical modeling techniques. These quantitative, predictive analysis methods enable the simulation of microbial growth and behavior *in silico*. . . . The ability to model regulatory events also has applications in the field of metabolic engineering.

The '754 application at page 1, para. 3 (emphasis added).

The above description sets forth that the entire application is directed to an *in silico* model, which requires a computer readable medium or media because *in silico* refers to computer and computational methods of modeling, and that the *in silico* model described therein contains regulatory events. The remainder of the '754 application is directed to how to make and use the regulatory *in silico* models described therein. For example, the '754 application sets forth at pages 4-12, a complete technical description for how to make and use the computer readable medium or media and perform the method of predicting a systemic property of a biochemical reaction network as claimed. Further, specific Examples that exemplify *in silico*

regulatory data structures, models and methods of determining a systemic property are described at, for example, pages 12-16. In particular, page 4, para. 3 through page 7, para. 1, describe a stoichiometric matrix and constraints as claimed. Pages 9 and 10 describe that flux balance analysis and linear programming can be used to carry out the simulated predictions of a data structure having a regulated reaction, and page 7, para. 2 through page 9, para. 1, and pages 11-12, describe how to incorporate regulated reactions into a data structure containing a stoichiometric matrix. In particular, page 8, para. 1 through page 9, para. 1, describes that a regulated reaction can be represented by Boolean logic and pages 11 and 12 describe that the regulatory event can be based on the passage of time. Applicants submit that these and other descriptions throughout the '754 application, and the related '028 application, are sufficient to satisfy the written description requirement for entitlement to priority. Accordingly, withdrawal of the rejection is respectfully requested.

#### **Rejections under 35 U.S.C. §101**

Applicants respectfully traverse the rejection of claims 1-65 and 70-74 under 35 U.S.C. §101 as allegedly being directed to non-statutory subject matter. With respect to the computer readable medium or media of claims 1-20 and 23-33, the Office alleges that the claims consist of a list of data and a constraint set for the data and include non-statutory forms of data storage such as carrier waves. The Office concludes that the claimed computer readable medium or media consist of non-functional descriptive data where none of the information causes the computer medium or media to perform any computer-implemented task.

As discussed during the personal interview with Examiner Zeman held August 22, 2006, the claimed subject matter does not require computer implementation in order to satisfy the requirements of §101. However, the claims have been amended as presented during the interview to recite both that the claimed data structure is stored on a computer readable medium or media and to include commands for determining a flux distribution that minimizes or maximizes an objective function when the constraint set is applied to the data structure. Further recited is that the claimed at least one flux distribution determines a systemic property of the biochemical reaction network.

Applicants previously pointed out that the claimed computer readable medium or media containing the recited data structure falls within both the definition of a data structure containing functionally descriptive material and within the Office's Guidelines exemplifying statutorily patentable data structures. The claimed data structure imparts functionality when employed as a computer component and it contains a specified relationship such that the claimed data structure does not constitute a data structure *per se*. See, for example, Response filed April 1, 2005, at pp. 16-17. Applicants additionally attempted to further prosecution of the subject application in their response filed April 1, 2005, by particularly showing that the claimed invention satisfies both the statutory classifications and the precedent set forth by the Supreme Court in *Diamond v. Charkrabarty* and the Federal Circuit in *State Street Bank & Trust Co. v. Signature Financial Group Inc.*.

In particular, Applicants further pointed out that any inquiry into the functionality of the claimed invention is necessarily framed under *State Street* where the inquiry is whether the claimed invention has a practical application. The *State Street* inquiry serves to exclude subject matter that falls under one of three judicial exceptions to patentability. Response filed April 1, 2005, at pp. 15-17.

Applicants additionally showed that the claimed invention falls directly within the scope of patentable subject matter under *State Street*, and as expressly described in the Examination Guidelines of the M.P.E.P. (e.g., M.P.E.P. § 2106 (IV)(B)(1)). Moreover, and as discussed during the personal interview on August 22, 2006, Applicants' previous remarks with respect to the M.P.E.P. Guidelines are consistent, and within the Office's current Interim Guidelines published November 22, 2005, because the entire rationale and express language of, for example, M.P.E.P. § 2106 (IV)(B)(1) is set forth in Annexes II-V of the Interim Guidelines. For example, Applicants previously stated:

Thus, according to these definitions [within the M.P.E.P. and the IEEE Standard Dictionary], a functional descriptive data structure is a relationship among data elements that imparts functionality when employed as a computer component.

The claimed computer readable medium or media containing the recited data structure falls within this definition and should be considered functional descriptive material and statutorily patentable. For example, the [claimed] data structure is contained on a computer readable medium or media and therefore is a

computer component. The claimed data structure also consists of a physical or logical relationship among data elements because it expressly claims relating a plurality of reactants to a plurality of reactions of a biochemical network. Further, the claimed computer readable medium or media containing the recited data structure also imparts functionality when employed as a computer component because [it] is used to determine a systemic property of a biochemical network.

Response filed April 1, 2005, at pp. 15-17 (emphasis added).

Applicants also have respectfully provided the Office with recent authority that overrules rejections based on a requirement that an invention must interact with a computer in the execution of a method (*In re Lundgren*, B.P.A.I. Case Nos. 2003-2088 (Sept. 28, 2005) (*Per Curium*)). The claimed Lundgren invention was directed to a method of compensating a manager. *Id.*, slip op. at p.1. The Examiner rejected the claimed invention for being directed to non-statutory subject matter allegedly because:

[B]oth the invention and the practical application to which it is directed to be outside the technological arts, namely an economic theory expressed as a mathematical algorithm without the disclosure or suggestion of computer, automated means, apparatus of any kind.

*Id.* slip op. at p.4 (emphasis added).

The requirement for a computer, an automated means or an apparatus in *Lundgren* was directly related to the Office's conclusion that the claimed invention was not required to interact with a computer. *In re Lundgren* dispelled any notion for requiring interaction with a computer to exist when the Court stated:

In *Musgrave*, the court reversed a rejection under 35 U.S.C. § 101 that the claims under review therein were non-statutory because it disagreed with the Board that "these claims . . . are directed to non-statutory processes merely because some or all of the steps therein can also be carried out in or with the aid of the human mind or because it may be necessary for one performing the processes to think."

*In re Lundgren*, slip op. at p.7 (emphasis added, citations omitted).

Therefore, The Board of Appeals and Interferences of the U.S. Patent and Trademark Office has overturned rejections attempting to require method claims to include machine or computer processing limitations such as the instant requirement for interaction with a computer.

*Id.* This decision by the U.S.P.T.O. overrules any rejection based on the alleged requirement for having computer implementation, such as the rejection above requiring performance of a computer-implemented task.

However, the claims clearly impart an interaction requiring a computer-implemented task. Therefore, in light of any of the applicable precedent, the claimed relationship of the data structure or the recitation in the claims that the data structure is stored on a computer readable medium or media and includes commands for determining a flux distribution that minimizes or maximizes an objective function when the constraint set is applied to the data structure, Applicants maintain that claims 1-20 and 23-33 satisfy the requirements of §101 for statutory patentable subject matter. Accordingly, withdrawal of this ground of rejection is respectfully requested.

With respect to the method for determining a systemic property of a biochemical reaction network of claims 34-65 and 70-75, the Office alleges that the claimed methods fail to produce a concrete, tangible and useful result. The Office concludes that the methods of the invention do not transform a physical object to a different state or produce a result that is communicated to a user.

As with the above rejection, Applicants do not concede that the Office's Interim Guidelines or the requirements set forth therein are the applicable authority for assessing statutory subject matter. Claims 34 and 71, and their dependents, are directed to a method for determining a systemic property of a biochemical reaction network. The method employs, *inter alia*, a data structure relating a plurality of reactants to reactions of a biochemical reaction network and a constraint set for determining at least one flux distribution that minimizes or maximizes an objective function when the constraint set is applied, the at least one flux distribution determines a systemic property of the biochemical reaction network. As described previously, and discussed during the personal interview held on August 22, 2006, the result yielding at least one flux distribution determinative of a systemic property of a biochemical reaction network constitutes a practical application under the Office's guidelines. Nevertheless, to further prosecution, the claims also now recite that the determined systemic property is provided to a user.

With respect to producing a result having a practical application, the result satisfies the Office's "useful result" criteria because it has a specific, substantial and credible utility. The utility of the claimed invention is specific to the subject matter claimed, and not general, because the claims recite that the at least one flux distribution determines a systemic property of a biochemical reaction network. Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility, Nov. 22, 2005, section IV.B.2.b., *citing* M.P.E.P. § 2107 (*see also* Revised Interim Utility Guidelines Training Materials at page 5 (1999)). The utility is substantial because it has a real world use, namely, predicting a systemic property of a biochemical reaction network, such as in a cell or organism for diagnostic or therapeutic purposes. *Id.* The utility also is credible because there is no reason for one skilled in the art to question the objective truth of the statement of utility and it is currently available for use. *Id.* Therefore, the claimed invention produces a useful result under the non-binding Interim Guidelines because it yields a specific, substantial and credible result.

Second, the claimed invention also satisfies the Office's "tangible result" criteria because it yields at least one flux distribution determinative of a systemic property of a biochemical reaction network. The Interim Guidelines correctly acknowledge that:

The tangible requirement does not necessarily mean that a claim must either be tied to a particular machine or apparatus or must operate to change articles or materials to a different state or thing.

Interim Guidelines, Nov. 22, 2005, section IV.B.2.b(2) (emphasis added); *see also In re Lundgren* cited in Applicants' previous response and discussed further above.

As Applicants have set forth on the record, there is no requirement for a claimed invention to be either tied to a particular machine or to transform a thing to a different state. The Office's own guidelines acknowledged this fact. Accordingly, Applicants respectfully request that any rejection based on this requirement be withdrawn.

Under the "tangible result" prong of the Office's guidelines, the requirement for a tangible result must also be differentiated from three judicial exceptions to patentability, which are: (1) laws of nature; (2) physical phenomena, and (3) abstract ideas. The guidelines further define the meaning of "tangible" to be opposite of "abstract."

With respect to the first two judicial exceptions listed above, the invention claims neither a law of nature nor a physical phenomena *per se*. Rather, the claimed invention is directed to a method for determining a systemic property of a biochemical reaction network having a data structure that relates a plurality of reactants to a plurality of reactions of a biochemical reaction network. The method for determining a systemic property further employs a constraint set, a variable constraint, a condition-dependent value and an objective function, all of which are used for determining at least one flux distribution that minimizes or maximizes an objective function when the constraint set is applied to the data structure. The at least one flux distribution is determinative of a systemic property of the biochemical reaction network. There is no recitation in this claim of merely a law of nature or a physical phenomena. Accordingly, the claimed invention cannot be statutory unpatentable under these two judicial exceptions.

Further, there is nothing in the claimed invention that constitutes a mere abstract idea. First, the claimed invention is more than just an idea because it claims a data structure having a relationship and a constraint set that, when applied to an objective function, determines at least one flux distribution that minimizes or maximizes the objective function and thereby determines a systemic property. Hence, the ability to predict a systemic property of a biochemical reaction network is more than an idea. Rather, it is an actual outcome.

Second, the claimed invention is not abstract. The term “abstract” is defined as:  
[c]onsidered apart from any application to a particular object or specific instance  
. . . . insufficiently factual . . . . having no reference to a thing or things --  
opposed to concrete. . . . Expressing a property, quality, attribute, or relation  
viewed apart from the other characteristics inhering in or constituting an object.

*Webster's Third New International Dictionary, Unabridged*. Merriam-Webster, 2002.  
<http://unabridged.merriam-webster.com> (21 Aug. 2006) (emphasis added).

As Applicants' have maintained, there is nothing abstract about the claimed invention. Rather, it is sufficiently factual because it recites a data structure containing a relationship of reactants and reactions and a constraint set that when applied to an objective function is determinative of a biochemical reaction network. Further, the claimed invention is not claimed apart from, or without reference to, a thing or to characteristics in an object because it specifically recites the requisite reactants, reactions and a relationship for a biochemical reaction



network such as those in a cell or organism. Accordingly, the invention is concrete and not abstract because it is sufficiently factual and does not recite purely theoretical ideas detached from a particular object. Therefore, the claimed invention also produces a tangible result under the non-binding Interim Guidelines because it does not claim a law of nature, a physical phenomena or merely abstract idea apart from any application to a particular object.

Finally, the claimed invention satisfies the Office's "concrete result" requirement. The Interim Guidelines define this prong as being the opposite of "concrete," which is "unrepeatable or unpredictable." Interim Guidelines, Nov. 22, 2005, section IV.B.2.b(3). Applicants respectfully submit that the invention claims determining at least one flux distribution that is determinative of a systemic property of a biochemical reaction network. Further, Applicants have provided detailed teachings and guidance throughout the application for how to make and use the invention to determine at least one flux distribution that is determinative of a systemic property of a biochemical reaction network. Therefore, the claimed invention further produces a concrete result under the non-binding Interim Guidelines because it yields a result that is determinative of a systemic property of a biochemical reaction network.

Therefore, in light of any of the applicable precedent as set forth above and in Applicants' previous Responses, the claimed practicable application having a useful, concrete and tangible result or the recitation in the claims that the determination step thereby provides the systemic property to a user, Applicants maintain that claims 34-65 and 70-75 satisfy the requirements of §101 for statutory patentable subject matter. Accordingly, withdrawal of the rejection is respectfully requested.

### **Rejections Under 35 U.S.C. § 112, First Paragraph**

Applicants respectfully traverse the rejection of claims 12-13, 30, 35-38 and 46-47 under 35 U.S.C. §112, first paragraph, as allegedly lacking written description. With respect to claims 12-13 and 46-47, the Office alleges that the specification fails to describe the concept of a data structure relating a plurality reactions that occur in a first cell population with a regulatory data structure representing events that occur in a second cell population. The Office further alleges that paragraph [0038] "makes clear [that the reactions are] within or about one cell;" that

paragraph [0135] “lists exemplary organisms which can be modeled,” and that paragraph [0136] “discusses the incorporation of a regulatory structure but does not provide support for the data structure.” Office Action mailed May 12, 2006, at page 6.

The test for adequate written description is whether a person of ordinary skill in the art would recognize that the applicant possessed what is claimed. *Noelle v. Lederman*, 355 F.3d 1343, 1348 (Fed. Cir. 2004) (citing *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991); *Enzo Biochem, Inc., v. Gen-Probe Inc.*, 296 F.3d 1316, 1328 (Fed. Cir. 2002) ([t]he specification must adequately describe the claimed invention so that one skilled in the art can recognize what is claimed).

Claims 12-13 are directed to a computer readable medium or media and claims 46-47 are directed to a method for determining a systemic property, wherein the claimed biochemical reaction network represents reactions that occur in a first cell in a population of cells and the claimed regulatory data structure represents events that occur in a second cell in the population.

As discussed during the personal interview on August 22, 2006, a fair reading of the entire application, including the exemplary paragraphs cited in Applicants’ previous Responses, provide sufficient support such that one skilled in the art would recognize what is claimed.

For example, paragraph [0033] teaches that that a regulatory data structure refers to first and second reactions related by a function that alters the flux through the second reaction by changing the value of a constraint on the second reaction.

Paragraph [0038] teaches that a biochemical reaction network of the claimed invention can be represented by a data structure relating reactants and reactions. The reactants can be assigned to different compartments. Described therein are a number of exemplary compartments, which include extracellular compartments such as where signal transduction molecules can be found during signaling events between cells.

Paragraph [0136] teaches use of the methods of the invention to model events occurring in different cells of an organism when it describes that the claimed methods can be used to simulate a variety of biological networks including signal transduction and physiological systems. Further, this paragraph expressly teaches that the claimed biochemical reaction network can represent reactions occurring in a first cell in a population of cells and the claimed

regulatory data structure can represent events that occur in a second cell in the population when it describes:

The incorporation of a regulatory structure with flux balance analysis and linear optimization can also be used to simulate the activity or function of other biological networks. Those skilled in the art will be able to apply the above-described models and methods in order to simulate a variety of biological networks including, for example, networks of a cell, group of cells, organ, organism or ecosystem. Activities for individual steps or processes in the network can be converted into a data structure that relates the particular step or process to the components they act upon. In addition, the activities can be constrained using constraints sets as described above. As an example, the methods can be used to simulate a signal transduction system as a flux of free energy through the system where interactions between signaling partners are represented as reactions and are constrained with respect to the amount of energy that flows from one partner to another. Regulation can be incorporated by varying the constraints with respect to effects of cross talk between signaling systems. Similarly, physiological systems can be simulated by creating data structures that correlate physiological functions with particular organ, tissues or cells and regulatory data structures or events can be incorporated to represent the effects of stimuli or insults such as hormones, pathogens or environmental conditions that affect the physiological system. Another example, is an ecosystem for which a data structure can be constructed that relates organisms and ecological processes, wherein regulation can include a representation of changes in environmental conditions.

Application at para. [0136] (emphasis added).

The above description directed to simulating groups of cells, an organ, organism, physiological system, ecosystem or signal transduction between partners exemplify a biochemical reaction network where reactions occurring in a first cell can be represented in one data structure and events occurring in a second cell of a population can be represented in a second regulatory data structure. Paragraph [0135] provides further support because it teaches that the invention can be used to model a variety of multi-cell populations, including eukaryotic organisms and the multicellular human organism.

Accordingly, the above paragraphs teach a regulatory data structure where one reaction alters the flux of another reaction and that data structures and biochemical networks can occur in different compartments. The different compartments can be intracellular, extracellular, between

groups of cells, an organ, organism, physiological system, ecosystem or signal transduction partners. These teachings and exemplifications provide sufficient support for the claimed invention and withdrawal of this ground of rejection is respectfully requested.

With respect to claim 30, the Office asserts that a confidence rating for the occurrence of a reaction is unsupported because the specification allegedly describes that other annotation information, which can be included in the claimed computer readable medium or media, is a level of confidence with which a reaction is believed to occur in a particular biochemical reaction network or organism.

While Applicants do not concede that the claimed term is unsupported by the cited language in the application, as discussed during the personal interview, Applicants have amended this claim to recite that the annotation includes a confidence level for occurrence of a reaction. In light of this amendment, Applicants submit that this ground of rejection is moot and respectfully request its withdrawal.

With respect to claims 35-38, the Office asserts that the claimed condition-dependent value and variable constraint that includes a value conditioned on the outcome of at least one reaction is unsupported because the application allegedly refers to regulatory events and variable function, rather than a value being conditioned on another element.

As noted above, and discussed during the personal interview, a condition-dependent value and variable constraint that include a value conditioned on the outcome of at least one reaction are sufficiently described in the application and are included in the teachings of regulatory events and a variable function. It is the value of a variable constraint, or condition-dependent value, that is changed in response to a regulatory event. The change in the value of the variable constraint is altered when acted on by a function specified by the regulatory event during simulation of the claimed model or method.

For example, independent claim 34 recites providing a condition-dependent value to the claimed variable constraint. Claims 35-39 further specify the origin of the condition-dependent value. Briefly, paragraph [0033] teaches that that a regulatory data structure refers to first and second reactions related by a function that alters the flux through the second reaction by changing the value of a constraint on the second reaction.

Paragraph [0049] further teaches that a variable constraint refers to a constraint that is capable of assuming any of a set of values in response to being acted upon by a function. Based on these teachings, claims 35, 36 and 37 are clearly supported because these claims recite that the condition-dependent value provided to the variable constraint of claim 34 results from one or more reactions specified in the data structure, from a regulatory event or from a temporal event when acted on by a function that alters the flux through a second reaction by changing the value of a constraint on the second reaction.

Paragraph [0049] further teaches that the function can correlate a constraint with at least one reaction, corresponding to changes regulating a reaction. Paragraph [0047] additionally teaches that the function can modify the flux through a reaction corresponding to a regulatory event where the modifier of flux through a reaction includes a condition such as time or an environmental condition. Additionally, the application explicitly teaches the claimed element further when it describes:

Since there are regulatory constraints on the network, the effects of these constraints can be taken into consideration in the context of the condition being examined to determine if there are additional constraints associated with regulation that will impact the reaction network's performance. Such constraints constitute condition-dependent constraints.

Application at para. [0066] (emphasis added).

The application further teaches that the value of the condition-dependent constraints are changed during simulation of a biochemical reaction network when it describes:

With the effects of the regulatory network taken into consideration and the condition-dependent constraints set to relevant values, the behavior of the biochemical reaction network can be simulated for the conditions considered.

Application at para. [0070].

Therefore, Applicants submit that claims 35-37 are sufficiently supported to satisfy the written description requirement of §112 because the origin of the condition-dependent value provided in step (c) of base claim 34, and because the application describes that a variable constraint can be derived from at least one reaction in the data structure or a regulatory or

temporal event of the claimed invention. Accordingly, Applicants respectfully request that this ground of rejection be withdrawn.

**Rejections Under 35 U.S.C. § 112, Second Paragraph**

Applicants respectfully traverse the rejection of claims 2-7, 9-16, 26-30, 32-33, 35-39, 48-50, 52, 55, 64-66 and 73 under 35 U.S.C. §112, second paragraph, as being indefinite for allegedly failing to further limit their base claims. Specifically, the Office alleges that the rejected dependent claims all modify an arrangement of non-functional descriptive material and allegedly do not modify the structure of the composition being claimed.

As discussed during the personal interview with Examiner Zeman on August 22, 2006, Applicants have pointed to the teachings in the application for each and every element in the rejected claims. In general, the rejected claims relate to the claimed regulatory data structure and variable constraint. As discussed during the interview, and as set forth above and previously discussed in the record, it is the value of a variable constraint that is changed in response to a regulatory event. The change in the value of the variable constraint is altered when acted on by a function specified by the regulatory event during simulation of the claimed model or method. Paragraph [0049] clearly teaches that the term "function" is used consistently with the meaning of the term as it is understood in the computer and mathematical art. Further, Applicants have amended the claims to include recitation of commands for determining a flux distribution when a constraint set is applied to the data structure that determines a systemic property of the biochemical reaction network, and to recite that the at least one flux distribution is determinative of determining a systemic property which thereby provides the systemic property of to a user. In light of the teachings in the specification and Applicants amendments, Applicants maintain that the meaning of the rejected terms are sufficiently clear to those skilled in the art. Accordingly, withdrawal of the rejection is respectfully requested.

**Rejections Under 35 U.S.C. § 102**

Applicants respectfully traverse the rejection of claims 1-3, 5-7, 17-20, 23-26, 29, 32-34, 40, 53-54, 56-61 and 64-66 under 35 U.S.C. §102(b) as allegedly anticipated by WO 00/46405 to

Palsson. Specifically, the Office alleges that the claimed invention constitutes non-functional descriptive material and is, therefore, anticipated by WO 00/46405. The Office further asserts that WO 00/46405 describes regulated reactions and variable constraints allegedly because it describes limiting constraints on various fluxes, interpreting the constraints to be variable and the reactions they relate to be regulated.

Claim 1 is directed to a computer readable medium or media having a data structure where at least one reaction is a regulated reaction and a constraint set having a variable constraint for the regulated reaction. Claim 34 is directed to a method for determining a systemic property of a biochemical reaction network which employs this data structure.

A finding of anticipation requires that the publication describe all of the elements of the claims. *C.R. Bard, Inc. v. M3 Sys., Inc.*, 157 F.3d 1340, 1349, 48 U.S.P.Q.2d 1225, (Fed. Cir. 1998) (quoting *Shearing v. Iolab Corp.*, 975 F.2d 1541, 1544-45, 24 U.S.P.Q.2d 1133, 1136 (Fed. Cir. 1992)). As discussed during the personal interview on August 22, 2006, Applicants submit that WO 00/46405 fails to describe a variable constraint for a regulated reaction as it is described and claimed in the subject application.

As set forth above, Applicants assert that the claimed invention satisfies the applicable precedent as well as the non-binding Interim Guidelines for statutory subject matter. The claims further recite commands for determining a flux distribution when a constraint set is applied to the data structure that determines a systemic property of the biochemical reaction network, and to recite that the at least one flux distribution is determinative of determining a systemic property which thereby provides the systemic property of to a user. Therefore, the claimed invention should properly be construed to contain all claimed elements. In particular, WO 00/46405 fails to describe a variable constraint for a regulated reaction as claimed and, therefore, cannot anticipate the invention as claimed.

Applicants further submit that WO 00/46405 does not describe a variable constraint for a regulated reaction as required by the claimed invention because WO 00/46405 does not describe a constraint that is generated from performance of the model or method as claimed. For example, paragraph [0033] teaches that that a regulatory data structure refers to first and second reactions related by a function that alters the flux through the second reaction by changing the value of a constraint on the second reaction. Paragraph [0049] teaches that a variable constraint

is "capable of assuming any of a set of values in response to being acted upon by a function." Further, paragraph [0061] teaches that the function that is altered which is specified in the commands that determine a systemic property and alters the claimed variable constraint can be, for example, Boolean logic. In particular, the application teaches:

A regulatory data structure can represent regulatory reactions as Boolean logic statements. For each reaction in the network a Boolean variable can be introduced (Reg-reaction). . . . A series of Boolean statements can then be introduced to mathematically represent the regulatory network.

Application at para. [0061] (emphasis added).

Thus, WO 00/46405 neither describes such a constraint dependent on a condition during determining a systemic property nor does WO 00/46405 describe any type of function such as Boolean logic that can perform such an action. Rather, the constraints referred to in WO 00/46405 are described as being set so as to provide limits to the linear equations (or linear programming equations) described therein (e.g., page 7, lines 19-27; page 3, lines 15-36). Therefore, WO 00/46405 cannot anticipate the invention as claimed because this reference fails to describe a variable constraint as described and claimed. Accordingly, withdrawal of the rejection is respectfully requested.

### **Rejections Under 35 U.S.C. § 103**

Applicants respectfully traverse the rejection of claims 1-33 under 35 U.S.C. §103(a) as allegedly obvious over Edwards et al. Specifically, the Office maintains that the claimed invention is considered to be non-functional descriptive material, alleging that Edwards et al. describe a computer readable medium containing lists of biological data and that the only structure required by the claimed invention are lists of data and lists of constraints.

To establish a *prima facie* case of obviousness, the Office must show that the prior art would have suggested the claimed invention to one of ordinary skill in the art and that it could have been carried out with a reasonable likelihood of success when viewed in the light of the prior art. *Brown & Williamson Tobacco v. Philip Morris*, 229 F.3d 1120, 1124 (Fed. Cir. 2000), accord *In re Royka*, 180 USPQ 580 (C.C.P.A. 1974) (to establish *prima facie* obviousness, all claim limitations must be taught or suggested by the prior art); M.P.E.P. §2143.03.



As discussed during the personal interview with Examiner Zeman, and as set forth above, the claimed invention satisfies the applicable precedent as well as the non-binding Interim Guidelines for statutory subject matter. The claims recite commands for determining a flux distribution when a constraint set is applied to the data structure that determines a systemic property of the biochemical reaction network, and further recite that the at least one flux distribution is determinative of determining a systemic property, thereby providing the systemic property to a user. Therefore, the claimed invention should properly be construed as statutory patentable subject matter, containing all recited claimed elements. Edwards et al. fail teach or suggest a variable constraint for a regulated reaction as claimed and, therefore, cannot render obvious the invention as claimed.

For example, Edwards et al. do not teach or suggest that that a regulatory data structure represents first and second reactions related by a function that alters the flux through the second reaction by changing the value of a constraint on the second reaction. Edwards et al., also do not teach or suggest that a variable constraint is capable of assuming any of a set of values in response to being acted upon by a function, nor does Edwards et al. teach or suggest that the function that is altered, which is specified in the claimed commands that determine a systemic property and alters the claimed variable constraint, can be, for example, Boolean logic. Edwards et al. is completely silent with respect to these elements of the claimed invention. Therefore, absent some teaching or suggestion of a regulatory data structure as claimed, Edwards et al. cannot render the claimed invention obvious. Accordingly, Applicants respectfully request withdrawal of the rejection.


**CONCLUSION**

In summary, for the reasons set forth herein, Applicants submit that the claims are in condition for allowance and respectfully request a notice to this effect. If the Examiner would like to discuss any of the issues raised in the Office Action, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Check number 583832 in the amount of \$1,080.00 is enclosed as payment for the five-month Petition for Extension of Time fee. No other fee is believed due in connection with the filing of this Response. However, in the event that any additional fee is due, the Commissioner is hereby authorized to charge any amounts required by this filing, or credit any overpayment, to Deposit Account No. 07-1896 referencing the above-identified attorney docket number. A duplicate copy of the Transmittal sheet is enclosed.

Respectfully submitted,

Date: November 8, 2006

  
for Lisa A. Haile, J.D., Ph.D.  
Registration No. 38,347  
Telephone: (858) 677-1456  
Facsimile: (858) 677-1465

Reg. No.  
45,517

DLA PIPER US LLP  
4365 Executive Drive, Suite 1100  
San Diego, California 92121-2133  
USPTO Customer Number 28213